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2. Patent application number *(The Patent Office will fill in this part)*	20 MAR 2003 0306472.2
3. Full name, address and postcode of the or of each applicant *(underline all surnames)*	AorTech International plc Phoenix Crescent Strathclyde Business Park Bellshill Lanarkshire, ML4 3NJ
Patents ADP number *(if you know it)*	772824900
If the applicant is a corporate body, give the country/state of its incorporation	United Kingdom
4. Title of the invention	"Valve"
5. Name of your agent *(if you have one)*	Murgitroyd & Company
"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*	Scotland House 165-169 Scotland Street Glasgow G5 8PL
Patents ADP number *(if you know it)*	1198015

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8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if: a) any applicant named in part 3 is not an inventor, or b) there is an inventor who is not named as an applicant, or c) any named applicant is a corporate body. See note (d))*	Yes

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Claim (s)	------
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Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*

Request for preliminary examination and search *(Patents Form 9/77)*

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Any other documents *(please specify)*

11. I/We request the grant of a patent on the basis of this application.

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Murgitroyd & Company 19 March 2003

12. Name and daytime telephone number of person to contact in the United Kingdom ROISIN MCNALLY 0141 307 8400

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"Valve"

The present invention relates to artificial heart valves, more particularly to flexible leaflet heart valves which are used to replace natural aortic or pulmonary valves of the heart.

Ideally artificial heart valves should work in a similar fashion to natural heart valves in that when blood flows in a particular direction the valve adopts an open position to permit blood flow through it, whereas when blood tries to flow in the opposite direction the valve adopts a closed position preventing the flow of blood in the reverse direction through the valve (regurgitation).

Natural heart valves use thin flexible tissue leaflets as the closing members. In the closed position the leaflets are arranged such that each leaflet contacts its neighbour. This arrangement serves to close the valve and prevent the back flow of blood through the valve. In the open position

the leaflets separate from each other and move radially towards the inner walls of the blood vessel in which the valve is located. This open configuration of the valve permits the flow of blood through the valve.

A number of artificial cardiac valves have been produced which comprise leaflets which open and close in a similar fashion to natural valve leaflets. However, although the artificial valves work in a similar manner to the natural valves, the geometries of the leaflets differ due to the properties of the materials used in the construction of the synthetic heart valves.

A number of factors have to be considered when designing artificial heart valves of similar design to natural heart valves. These include the pressure gradient required to open and close the leaflets of the valve, regurgitation, blood handling and durability of the valve.

The leaflets of both natural and synthetic heart valves must be capable of withstanding a high back pressure across the valve when they are in the closed position, yet be capable of opening with a minimum of pressure across the valve in the forward direction of blood flow.

This is necessary to ensure correct operation of the valve even when blood flow is low. Further the valve should open quickly and as wide as possible

when blood flows in the desired direction. The maximum orifice of the valve in the open position is generally dictated by the width of the valve.

In order to minimise closing regurgitation (reverse blood flow through the closing valve) in the closed position of the valve, the free edges of the leaflets should come together to form a seal to minimise the reverse flow of blood.

The valve design and the materials used for valve construction should minimise the activation of both the coagulation system and platelets. The flow of blood through the valve should avoid exposing blood to either regions of high shear or relative stasis.

In addition, in order to be suitable for implantation, synthetic valves should be sufficiently durable such that they are clinically functional for at least 20 years. Durability of the synthetic leaflets depends on the materials from which the leaflets are constructed and also the stresses to which the leaflets are subjected during use. Although several materials have suitable hydrodynamic properties, many valves constructed using materials with suitable hydrodynamic properties fail during use, due to fatigue caused by the repeated stresses of cycling from a closed to an open position.

Conventional heart valves typically comprise an annular frame disposed perpendicular to the blood

flow. The annular frame generally has three posts extending in the downstream direction defining three generally U-Shaped openings or scallops between the posts. The leaflets are attached to the frame between the posts along the edges of the scallops and are unattached at the free edges of the leaflets adjacent to the downstream ends of the posts.

A valve design, comprising a leaflet geometry which was elliptical in the radial direction and hyperbolic in the circumferential direction in the closed valve position, with leaflets dip-coated from non-biostable polyurethane solutions onto injection-moulded polyurethane frames has attained durabilities in excess of 800 million cycles during *in vitro* fatigue testing (Mackay TG, Wheatley DJ, Bernacca GM, Hindle CS, Fisher AC. New polyurethane heart valve prosthesis: design, manufacture and evaluation. *Biomaterials* 1996; 17:1857-1863; Mackay TG, Bernacca GM, Wheatley DJ, Fisher AC, Hindle CS. *In vitro* function and durability assessment of a polyurethane heart valve prosthesis. *Artificial Organs* 1996; 20:1017-1025; Bernacca GM, Mackay TG, Wheatley DJ. *In vitro* function and durability of a polyurethane heart valve: material considerations. *J Heart Valve Dis* 1996; 5:538-542; Bernacca GM, Mackay TG, Wilkinson R, Wheatley DJ. Polyurethane heart valves: fatigue failure, calcification and polyurethane structure. *J Biomed Mater Res* 1997; 34:371-379; Bernacca GM, Mackay TG, Gulbransen MJ, Donn AW, Wheatley DJ. Polyurethane heart valve durability: effects of leaflet thickness. *Int J Artif Organs* 1997; 20:327-331.). However, this

valve design became unacceptably stenotic in small sizes. Thus, a redesign was effected, changing the hyperbolic angle from the free edge to the leaflet base, and replacing the injection-moulded frame with a rigid, high modulus polymer frame. This redesign permitted the use of a thinner frame, thus increasing valve orifice area. This valve design, with a non-biostable polyurethane leaflet material, was implanted in a growing sheep model. Over the six month implant period the region close to the frame posts on the inflow side of the valve, at which full leaflet opening was not achieved, suffered a local accumulation of thrombus (Bernacca GM, Raco L, Mackay TG, Wheatley DJ. Durability and function of a polyurethane heart valve after six months *in vivo*. Presented at the XII World Congress of International Society for Artificial Organs and XXVI Congress of the European Society for Artificial Organs, Edinburgh, August 1999. Wheatley DJ, Raco L, Bernacca GM, Sim I, Belcher PR, Boyd JS. Polyurethane: material for the next generation of heart valve prostheses? Eur. J. Cardio-Thorac. Surg. 2000; 17; 440-448). This valve design used non-biostable polyurethane, which had tolerable mechanical durability, but which showed signs of polymer degradation after six months *in vivo*.

International Patent Application WO 98/32400 entitled "Heart Valve Prosthesis" discloses a further design, using closed leaflet geometry, comprising essentially a trileaflet valve with leaflets moulded in a geometry derived from a sphere

towards the free edge and a cone towards the base of the leaflets. The spherical surface, defined by its radius, is intended to provide a tight seal when the leaflets are under back pressure, with ready opening provided by the conical segment, defined by its half-angle, at the base of the leaflets. It is stated that where the spherical portion is located at the leaflet base, an advantage is provided in terms of the stress distribution when the valve is closed and under back pressure.

U.S. Patent No. 5,376,113 entitled "Closing Member Having Flexible Closing Elements, Especially a Heart Valve" issued December 27, 1994 to Jansen et al. discloses a method of producing flexible heart valve leaflets using leaflets attached to a base ring with posts extending from this upon which the leaflets are mounted. The leaflets are formed with the base ring in an expanded position, being effectively of planar sheets of polymer, which become flaccid on contraction of the ring. The resulting valve is able to maintain both a stable open and a stable closed position in the absence of any pulsatile pressure, though in the neutral unloaded position the valve leaflets contain bending stresses. As a consequence of manufacturing the valve from substantially planar sheets, the included angle between the leaflets at the free edge where they attach to the frame is 60° for a three leaflet valve.

U.S. Patent No. 5,500,016 entitled "Artificial Heart Valve" discloses a valve having a leaflet shape

defined by the mathematical equation $z^2 + y^2 = 2RL(x-g)-\alpha(x-g)^2$, where g is the offset of the leaflet from the frame, RL is the radius of curvature of the leaflet at (g,0,0) and α is the shape parameter and is >0 and <1.

A valve design having a partially open configuration when the valve is not subject to a pressure gradient, but assuming a fully-open position during forward flow is disclosed in International Patent Application WO 97/41808 entitled "Method for Producing Heart Valves". The valve may be a polyurethane trileaflet valve and is contained within a cylindrical outer sleeve.

International Patent Application WO 01/41679 discloses a heart valve wherein the leaflets have been designed to facilitate wash out of the whole leaflet orifice including the area close to the frame posts. This Application teaches that stresses are highest in the region of the commisures where loads are transmitted to the stent, but they are reduced when the belly of the leaflet is as low as practicable in the closed valve. To ensure a belly in the leaflet, the above application indicates that there must be sufficient material in the leaflet. Further this application indicates that under back pressure, in the closed position, the shape of the leaflet can be defined by elliptical or hyperbolic coordinates.

A number of designs have been suggested for use in cardiac heart valves to ensure that the heart valves have sufficient leaflet material such that the valve is capable of opening as wide as the maximum possible orifice of the valve, that such opening requires as little energy as possible and further that regurgitation of blood through the valve is minimised.

However, the designs which have been previously described generally have not considered the stresses applied to the leaflets during the cycling of opening and closing of the valve.

It would be advantageous to provide a synthetic valve leaflet geometry that minimises the stresses present in the leaflets of the valve during cycling from the closed to the open position and back to the closed position increase the lifetime of the synthetic leaflets.

According to the present invention there is provided a cardiac valve prosthesis comprising:

a frame and at least two flexible leaflets;

wherein the frame comprises an annular portion which, in use, is disposed substantially perpendicular to the blood flow, the frame having first and second ends, one of the ends defining at least two scalloped edge portions separated and defined by at least two posts,

each leaflet being attached to the frame along a scalloped edge portion and being movable between an open and a closed position,

each of the at least two leaflets having a blood inlet side, a blood outlet side and at least one free edge, the at least two leaflets being in a closed position when fluid pressure is applied to the outlet side such that the at least one free edge of a first leaflet is urged towards the at least one free edge of a second or further leaflet, and the at least two leaflets being in an open position when fluid pressure is applied to the blood inlet side of the at least two leaflets such that the at least one free edge of the first leaflet is urged away from the at least one free edge of the second or further leaflet;

wherein in a first plane perpendicular to the blood flow axis the length of each leaflet in a circumferential direction (XY) between the posts at any position along the longitudinal axis (Z) of a post is defined by a parabolic function.

Preferably the length of a leaflet in the circumferential direction (XY) between the posts at any position along the longitudinal axis (Z) of a post (Z) is defined by the function:

Function of a parabola

$$Y_z = \left(\frac{4R}{L_z^2}\right)x.(L_z - x)$$

Wherein Y_z = Y offset at a particular co-ordinate X and Z

R = parabolic maximum

L_z = straight line distance between a first post and a second post of the frame at a height Z

x = distance from origin of post towards another post

$$\text{Length} = \int_0^l \sqrt{1+\left(\frac{dy}{dx}\right)^2}\,dx$$

It is understood that a parabolic function includes any pseudotrigonmetric, pseudoelliptical, smooth function or table of values that describe a geometry which is substantially parabolic.

The use of a pseudo function to describe a parabolic function will be obvious to one skilled in the art.

Preferably the cast shape of the leaflet in the circumferential direction (XY) at any position along the longitudinal axis (Z) of a post is defined by a first wave having a first frequency.

Preferably the first wave is a sinusoidal wave.

More preferably the cast shape of the leaflet in the circumferential direction (XY) at any position along the longitudinal axis (Z) of a post is defined by at least two waves of differing frequency, which form a composite wave.

Preferably the length of the leaflet in the circumferential direction (XY) between the posts at any position along the longitudinal axis (Z) of a post is defined by a parabolic function and at least one correction factor.

Preferably a correction factor is used to compensate for inward movement of the prosthesis posts on closure of the valve.

Preferably a correction factor is used to compensate for stretch in leaflet material on closure of the valve.

Preferably a correction factor is used to compensate for movement in the notional point of coincidence of the leaflets.

Preferably the first wave is asymmetric about the vertical mid plane parallel to and intersecting the blood flow axis of the leaflets.

Preferably the composite wave is asymmetric about the vertical mid plane parallel to and intersecting the blood flow axis of the leaflets.

Preferably the valve comprises three leaflets.

Preferably the frame has first and second ends, the first end defining at least three scalloped edge portions separated by at least three posts, each leaflet attached to the frame along a corresponding scalloped edge portion.

Preferably the three posts are rotationally symmetrically distributed around the circumference of the frame.

Preferably the frame is a collapsible stent.

Preferably the collapsible stent can be delivered to the patient by percutaneous delivery.

More preferably the collapsible stent can be moved from a collapsed to an erect position using an inflatable balloon when the stent is suitably located in the patient.

According to a second aspect of the invention there is a method of making a cardiac valve prosthesis wherein the method comprises;

- providing a forming element having at least two leaflet-forming surfaces wherein the forming surfaces are such that the length in the circumferential direction (XY) of the leaflet-forming surface is defined by a parabolic function,

- engaging the forming element with the frame,
- applying a coating over the frame and the engaged forming element, the coating binding to the frame, the coating over the leaflet-forming surfaces forming at least two flexible leaflets, the at least two flexible leaflets having a length in the circumferential direction (XY) defined by a parabolic function and a surface contour such that when the first leaflet is in the neutral position an intersection of the first leaflet with at least one plane perpendicular to the blood flow axis forms a first wave having a first frequency,
- disengaging the frame from the forming element.

The leaflets are in a neutral position intermediate to the open and closed position in the absence of fluid pressure being applied to the leaflets.

Preferably there is provided a method of making a cardiac valve prosthesis wherein the method comprises;

- providing a forming element having at least two leaflet-forming surfaces wherein the forming surfaces are such that the length in the circumferential direction (XY) of the leaflet-forming surface is defined by a parabolic function,
- engaging the forming element with the frame,

- applying a coating over the frame and the engaged forming element, the coating binding to the frame, the coating over the leaflet-forming surfaces forming at least two flexible leaflets, the at least two flexible leaflets having a length in the circumferential direction (XY) defined by a parabolic function and a surface contour such that when the first leaflet is in the neutral position an intersection of the first leaflet with at least one plane perpendicular to the blood flow axis forms a composite wave defined by at least two waves of differing frequency,
- disengaging the frame from the forming element.

Preferably there is provided a method of making a cardiac valve prosthesis wherein the method comprises;

- providing a forming element having three leaflet-forming surfaces wherein the forming surfaces are such that the length in the circumferential direction (XY) of the leaflet-forming surface is defined by a parabolic function,
- engaging the forming element with the frame,
- applying a coating over the frame and the engaged forming element, the coating binding to the frame, the coating over the leaflet-forming surfaces forming three flexible leaflets, the three flexible leaflets each having a length in

the circumferential direction (XY) defined by a parabolic function and a surface contour such that when the first leaflet is in the neutral position an intersection of the first leaflet with at least one plane perpendicular to the blood flow axis forms a wave defined by at least a first wave, having a first frequency,

- disengaging the frame from the forming element.

Preferably there is provided a method of making a cardiac valve prosthesis wherein the method comprises;

- providing a forming element having three leaflet-forming surfaces wherein the forming surfaces are such that the length in the circumferential direction (XY) of the leaflet-forming surface is defined by a parabolic function,
- engaging the forming element with the frame,
- applying a coating over the frame and the engaged forming element, the coating binding to the frame, the coating over the leaflet forming surfaces forming three flexible leaflets, the three flexible leaflets each having a length in the circumferential direction (XY) defined by a parabolic function and a surface contour such that when the first leaflet is in the neutral position an intersection of the first leaflet with at least one plane perpendicular to the blood flow axis forms a composite wave defined by at least two waves of differing frequency,

- disengaging the frame from the forming element.

It will be appreciated by those skilled in the art that leaflets of appropriate lengths and shape can be formed using dip moulding, conventional injection moulding, reaction injection moulding or compression moulding.

Preferably the method further comprises trimming the free edge of at least one leaflet.

More preferably the method further comprises trimming the free edge of at least one leaflet in the longitudinal direction (Z) of the leaflet.

More preferably the free edge of the leaflet is trimmed such that in the longitudinal direction (Z) the free edge of at least one leaflet is parabolic.

Preferably the free edge of at least one leaflet is parabolic in the longitudinal direction toward the second end of the frame such that the maximum depth of the parabolic cut is between 50μm to 1000μm lower than the notional free edge of the leaflet.

The leaflet has a top and bottom, the bottom of the leaflet being attached to the scalloped portion.

The top of the leaflet may extend beyond the tip of the posts of the frame e.g. by up to 1500 μm from the tip of the posts.

The notional free edge is defined as the free edge of the leaflet prior to trimming. The notional free edge may extend between the posts at a longitudinal height of between 0 to 1500 μm from the tip of the posts.

Preferably at least one leaflet has different thicknesses along a cross section defined by the intersection of a plane perpendicular to the blood flow axis.

More preferably the thickness of the cross section of at least one leaflet in the XY plane, defined by the intersection of a plane perpendicular to the blood flow axis, changes gradually and substantially continuously from a thickest portion where the leaflet is conjoined to the frame to a thinnest portion at the midpoint of the XY plane of the leaflet.

A problem associated with the design of synthetic heart valves is that changing the diameter of the valve or height of the posts of the frame affects the calculation of leaflet geometry. In order to overcome the effects of valve diameter or post heights on leaflet geometry, geometric scaling is typically employed.

Preferably the functions described herein can be used irrespective of valve diameter or the height of the posts of the frame, to obtain suitable leaflet

geometry and does not require the use of geometric scaling.

Therefore functions disclosed by the present Application which describe length in the circumferential direction (XY) of a leaflet e.g. the leaflet geometry optimised for a 27mm inside diameter of stent can be used to describe the length in the circumferential direction (XY) leaflet geometry for a stent of different diameter e.g. 17mm inside diameter stent.

This makes the design and manufacture of valves of different diameters more convenient.

An embodiment of the present invention will now be described, by way of example only with reference to the accompanying drawings wherein;

Figure 1 is a plan view of a trileaflet heart valve in the closed position;

Figure 2a is a perspective view of an embodiment of a trileaflet heart valve of the present invention in a semi-closed position;

Figure 2b is a perspective view of a prior art trileaflet heart valve in a semi-closed position;

Figure 3 is a plan view of an embodiment of a trileaflet heart valve of the present invention in a semi-closed position;

Figure 4a is a plan view of a prior art trileaflet heart valve in a fully open position;

Figure 4b is a plan view of a prior art trileaflet heart valve as shown in figure 4a in a fully closed position;

Figure 4c is a plan view of an embodiment of a trileaflet heart valve according to the present invention in a fully open position;

Figure 4d is a plan view of an embodiment of a trileaflet heart valve according to the present invention as shown in figure 4c in a fully closed position;

Figure 5a is a cross section of the valve as shown in figure 2a along line 3-3;

Figure 5b is a cross section of the prior art valve as shown in figure 2b along line 3-3;

Figure 6 is a plan view illustration of an embodiment of a trileaflet heart valve of the present invention;

Figure 7a shows a partial cross section of a post of an embodiment of a trileaflet heart valve of the present invention in the open position (II) and the closed position (I) of the valve;

Figure 7b shows the a partial cross section of an embodiment of a leaflet of the present invention along the vertical midplane in the open position (II) and closed position (I) of the valve;

Figure 7c shows the a partial cross section of a post of a prior art valve in the open position (II) and closed position (I) of the valve;

Figure 7d shows the a partial cross section of a leaflet of a prior art valve along the vertical midplane in the open (II) and closed (I) position of the valve;

Figure 8a shows the principal stress envelope present in a prior art heart valve leaflet;

Figure 8b shows the strain energy release present in a prior art heart valve leaflet in the X axis from a closed to open position;

Figure 8c shows the strain energy release present in a prior art heart valve leaflet in the Y axis from a closed to open position;

Figure 8d shows the resultant strain energy release present in a prior art heart valve during cycling from a closed to open position;

Figure 9a shows the principal stress envelope present in an embodiment of a heart valve according to the present invention;

Figure 9b shows the strain energy release present in an embodiment of a heart valve according to the present invention in the X axis from a closed to open position;

Figure 9c shows the strain energy release present in an embodiment of a heart valve leaflet according to the present invention in the Y axis from a closed to open position;

Figure 9d shows the resultant strain energy release present in an embodiment of a heart valve leaflet according to the present invention during cycling from a closed to open position;

Figure 10 is an illustration of an embodiment of one leaflet according to the present invention;

Figure 11 is a diagrammatic representation of a prior art leaflet moving from a semi-closed (a) to successively more open position (b) and (c)

to a fully open position (d) illustrating the formation of a bubble or buckle;

Figure 12 illustrates the shape of the leaflet being defined by a first wave further to determination of the circumferential length of the leaflet; and

Figure 13 is graph of Cardiac Output (l/min) against mean Pressure Gradient (mmHg).

As previously discussed, a number of designs have been suggested for use in cardiac heart valves to ensure that the heart valves have sufficient leaflet material such that the valve is capable of opening as wide as possible to the maximum orifice of the valve, and that such opening requires as little energy as possible and further that regurgitation of blood through the valve is minimised.

In order to minimise the regurgitation of blood it has been suggested that the free edge of the valve is spherical in geometry to ensure that the free leaflet edges are able to come together and seal against one another.

US Patent 5,500,016 discloses a leaflet defined by the equation:

$$z^2 + y^2 = 2RL\ (x-g) - \alpha(x-g)^2$$

to describe the geometry of the leaflets. As Z, defines the shape of the leaflet in the blood flow axis and as Z is defined as z^2 then a leaflet defined by the above would have a spherical geometry in the axis parallel to blood flow. International Patent Application WO 98/32400 discloses that spherical surfaces at the leaflet edges seal more effectively than planar or conical surfaces. International Application WO 01/41679 discloses that stresses are highest in the region of the comissures where loads are transmitted to the stent, but they are reduced when the belly of the leaflet is as low as practicable in the closed valve.

In addition International Application WO 98/32400 also suggests that it is advantageous to provide a spherical portion of leaflet adjacent to the base of the leaflet as it confers advantages in the stress distribution when the valve is closed and pressure is greater downstream than upstream.

The prior art teaches that leaflets of heart valves should have considerable excess material in the vertical axis Z, parallel to the blood flow to enable a suitable seal to be achieved at the free edge of the leaflet and to reduce the stress present in the leaflet during open and closing.

As shown in figure 1 and figure 2a, a preferred embodiment of the heart valve prosthesis 8 of the present invention comprises a stent or frame 10 which is substantially cylindrical. The frame has a

first end 12 and second end 14. The first end 12 comprises three scalloped edge portions 16a, 16b and 16c separated by three posts 18, each post having a tip 20. The cardiac valve further comprises three leaflets 30. Each leaflet 30 has a fixed edge 32 joined to a respective scalloped edge 16a, 16b or 16c of the frame 10 and a free edge 34 which extends substantially between the tips 20 of the posts 18.

The leaflets 30 are configured to be movable from an open to a closed position and from a closed to open position. In an aortic position (when the prosthesis is positioned at the site of the aortic valve), the leaflets 30 have a blood inlet side 36 and a blood outlet side 38 and are in the closed position when fluid pressure is applied to the outlet side 38 i.e. by the blood of the aortic artery and in the open position when fluid pressure is applied to the inlet side 36 i.e. by the blood of the ventricle. The leaflets are in a neutral position intermediate to the open and closed position in the absence of fluid pressure being applied to the leaflets.

Where the valve is being used in a mitral position, between the left atrium and left ventricle of the heart, the orientation of the valve is the opposite to that described above such that blood flow from the left atrium moves the leaflets to an open position, the leaflets opening towards the left ventricle to allow blood to flow into the left ventricle. Back pressure from blood flow from the

left ventricle towards the left atrium causes the mitral valve to close to minimise regurgitation.

In figure 5b which is a sectional view along line 3-3 illustrating the closed position of a leaflet of a valve of the prior art, a 'belly' portion 40 exists in the mid portion of the leaflet. This 'belly' portion between the free edge and the central portion of the leaflet causes leaflets of the prior art to have a double curvature, a curve in XY and a curve in Z. Further, the 'belly' shape 40 causes leaflets of the prior art to be almost concave in shape when viewed in cross section along the vertical midplane of the leaflet.

As shown in figure 5a which is a sectional view of the valve of the present invention along line 3-3 as shown in figure 2a, no 'belly' is present in the leaflets and in Z the leaflet in the closed position is substantially linear.

The prior art design including a 'belly' portion was favoured as it was thought to maximise sealing of the valve at the free edge and minimise regurgitation.

However, the double curvature, which comprises curvature in XY plane and in Z plane results in excess leaflet material at both the open and closed position which promotes the formation of a bubble or buckle 50 in the leaflet material (as shown in

figure 11) during movement from a closed to open position.

This excess material is shown most clearly by comparing figure 7d which shows a cross section of the valve along the vertical midplane (line I-I of figure 2b) of the leaflet 30 parallel to the blood flow axis.in a prior art leaflet with figure 7b which shows a cross section along the vertical midplane (line I-I of figure 2a) of a leaflet of the present invention. This comparison clearly shows that the leaflet 30 of the present Application does not display a belly region 40. Indeed the cross section shown in figure 7b indicates that the leaflet shape of the present invention is substantially linear in the vertical direction in both the open and closed valve positions.

To determine the circumferential length of material in XY to remove the 'belly' 40 observed in prior art leaflets, the length in the circumferential direction (XY) of the leaflet for any position in z must be determined, which still allows suitable opening and closure of the valve.

As shown in figure 6 the material of the leaflet must extend between the posts 18 such that in a closed position the free edge of the leaflets 34 come together at point 42 to minimise regurgitation of blood through the valve.

This circumferential length (XY) can be mathematically defined using a parabolic function.

Function of a parabola

$$Y_z = \left(\frac{4R}{L_z^{\,2}}\right) x.(L_z - x)$$

Wherein Y_z = Y offset at a particular co-ordinate X and Z

R = parabolic maximum

L_z = straight line distance between a first post and a second post of the frame at a height Z

X = distance from origin of post towards another post

To calculate the circumferential length (XY) at a height point of the posts for a leaflet defined in the circumferential (XY) direction by a parabolic function the following function can be used:

$$\text{length of parabolic curve} = \int_0^l \sqrt{1+\left(\frac{dy}{dx}\right)^2}\, dx$$

This allows a circumferential length (XY) to be determined at each height point in Z.

Thus as shown in figure 10 the circumferential length (XY) can be determined at Z1, Z2, Z3 …Zn.

The length of the leaflet in the circumferential direction (XY) is calculated and repeated in the radial direction (Z) to provide the complete geometry of the leaflet.

As the scallop edge 32 of the frame 10 as defined by the posts 18 of the frame is known, then a leaflet 30 can be defined by determining the distance between the two posts 18 at several height points in Z (where Z is a particular height along the posts). This post to post distance can then be used in the equation detailed above to generate a parabola (P) at each height point. Due to the scallop shape 32 defined by the posts 18 the circumferential length of the leaflet in XY will decrease moving from the first end at the tip 20 of the posts toward the second end of the frame 14 at the base of the posts. The more height points which are chosen, the more lengths (P) can be calculated along Z. If a large number of height points are chosen the lengths determined by the parabolic function moving from the tip of the posts to the base will vary in a substantially linear fashion.

The leaflets 30 of a valve 8 which are of circumferential length (XY) as determined using the above parabolic function will meet at the free edge 34 of the leaflet 30, but will not meet significantly at points lower than the free edge 34. The meeting of the leaflets at the free edge allows regurgitation to be minimised without including

excess material or a belly region 40 in the leaflets 30.

The circumferential length (XY) can be further adjusted to take account of factors which occur during cycling of the heart valve. These factors include inward movement of the posts 18 of the frame 10 due to pressure on the leaflets 30 during closing of the valve. The amount of inward movement of the posts 18 of the frame 10 is influenced by the rigidity of the frame 10 and the pressure exerted on the valve. The tips 20 of the posts 18 of the frame 10 move to a greater extent than the base of the posts and as the scallop geometry between the posts 18 of the frame 10 is accurately known this differential movement can be taken into account when determining the optimal circumferential length (P) of XY in the leaflet 30.

In addition to the posts 18 of the frame 10 moving toward each other during closure, the posts 18 also move towards the centre point 42 where the leaflets meet or the point of coincidence. The circumferential length XY of the leaflet can be adjusted to account for this movement.

The material of the leaflet 30 typically has some degree of elasticity and will stretch in response to blood flow pressure. This stretching can again be taken into account in determining the lengths of the leaflet 30 to ensure that a belly region 40 of the valve is minimised.

As shown in figure 8a, analysis of the stresses over time incurred by heart valves during the cycling process has revealed that the principal area of stress 60 in existing cardiac valves is found close to the midpoint of the free edge of the leaflets.

Using the data from figure 8a, strain energy release in X and Y, as shown in figures 8b and 8c respectively can be determined. Figure 8b shows that leaflets of the prior art have a vertical predisposition to defect propagation 62 at the free edge 34. Figure 8c indicates that leaflets have a predisposition to defect in the lateral dimension, at an area 64 in the leaflet 30 lower than the free edge of the leaflet 34, the lower area being located above the central portion of the leaflet. In tests during cycling of cardiac valves it has been found that over time, the stress in this lower area promotes failure of defects in the material to occur. These defects can cause valve failure.

The present invention has shown that analysis of the dynamics of existing valves during the cycling process has determined that the stress in this lower area is caused by the leaflets requiring to change the direction of their surface curvature during cycling.

In particular, as shown in figure 11, on cycling from a closed to an open position a region lower than the free edge forms a bubble like formation or

buckle 50 on the surface of the leaflet which is opposite in direction to the curvature of the surface of the rest of the leaflet.

On moving from the closed to open position the bubble like formation 50 is forced to become inverted such that it projects in an opposite direction causing a whip like action in the leaflet 30. This whip like action promotes high stresses in the area lower than the free edge 34 of the leaflet, as shown in figures 8a, 8b, 8c and 8d.

The inventor has surprisingly determined, as shown in figure 9a, that the principal stress envelope in relation to the valve as described in the present application, wherein the circumferential length XY of the leaflet at any point in Z is defined as a parabolic function, is decreased across the whole of the valve. In particular strain energy release in X and Y, as shown in figures 9b and 9c respectively, in relation to the valve of the present invention indicates that a leaflet wherein the circumferential lengths XY are determined by a parabolic function has minimised predisposition to defect propagation in the lateral dimension at an area in the leaflet lower than the free edge of the leaflet and above the central portion.

A reduction in the predisposition to defect propagation in the lateral dimension at an area in the leaflet between the free edge of the leaflet and the central portion in the leaflet of the present

invention is observed because there is less excess material and thus minimal belly in the leaflet of the present design.

On moving from the closed to open position a bubble like formation 50 is no longer created and thus a whip like action does not occur in the leaflet. As discussed, it is this whip like action which has been determined to promote high stresses in the area lower than the free edge of the leaflet. As illustrated by comparing figures 8a and 9a, in contrast to the valves of the prior art, uniform principle stress distribution, is observed across the surface of the leaflet of the valve described in the present Application.

Minimisation of the regions of stress in the leaflet, during cycling of the leaflet, will increase the durability of the leaflet.

Use of a parabolic function to determine the circumferential lengths XY of the leaflet at each height point in Z causes the vertical distribution of lengths of the leaflet to be substantially linear at the fully open and closed position.

It will be appreciated by those in the art that other functions with the addition of suitable modifying factors could be used to derive a function which substantially describes a parabola and which leads to the vertical distribution of lengths of the leaflet to be substantially linear at the fully open

and closed position, but which is based on for instance an elliptical function.

As discussed, additional parameters may be included in the parabolic function used to determine the circumferential lengths XY of the leaflet. These additional factors may account for movement in the posts of the stent, elasticity of the leaflet material during movement of the leaflets from a closed to an open position or other factors which occur during cycling which influence the length of the leaflet require to allow closure.

The function described above explicitly determines lateral lengths of the parabolic curve at any height point in Z which is along a post of the frame. In view of this the above function can be applied to any diameter of valve or valves with different heights of posts, without the need for geometric scaling. This means that different dimensions of valves can be manufactured with the same leaflet geometry without further undue experimentation.

The surface contour of the leaflets 30 of the embodiment described are such that in a fully open position, the intersection of the leaflets of the valve perpendicular to the blood flow axis, forms a substantially cylindrical shape.

In addition to the above, it has also been determined that stress at the free edge of the leaflet, as shown in figure 8a, can be further

reduced by trimming the free edge 34 of the leaflet in the longitudinal direction (Z) such that the free edge is substantially parabolic 70, with the maximum depth of the parabola being furthest from the notional untrimmed free edge 74. The maximum depth of the parabola is generally located at the midpoint of the free edge 72 (figure 9a). Figure 9a shows the effect of introducing a parabolic curve in the vertical direction of the free edge. Comparison of figures 8b, 8c and 8d with 9b, 9c and 9d shows that the strain energy release at the free edge is significantly reduced through the introduction of the parabola in the longitudinal direction (Z).

Ideally the notional free edge 74 is trimmed in a parabolic curve, wherein the maximum depth 72 of the parabola 70 is between 50μm to 1000μm lower than the notional untrimmed free edge 74.

A different shape of cut, trim or notch can be introduced in the free edge to decrease the stress at the free edge. However, particular shapes of cuts, trims or notches may introduce defects into the leaflet which would decrease the leaflets durability to stress. A parabolic trim as described is therefore advantageous in that focal points of stress are not introduced to the free edge of the leaflet.

Leaflets of the geometry described herein can be produced using methods known in the art such as

injection moulding, reaction injection moulding, compression moulding or dip moulding.

As discussed the circumferential length XY of the leaflet at any height point in Z along the post of the frame is explicitly provided by the function described above. On determining the length of the leaflet at each point in Z to minimise the formation of a belly in the leaflet, the shape of the leaflet in the circumferential direction can be defined by at least one wave 80. As shown in figure 12, further to determining the circumferential length determined at a chosen point in Z and applying appropriate correction factors to determine a final XY length at that point in Z, the shape of the leaflet is then defined as a wave.

As shown in figure 13, surprisingly, in addition to reducing the lateral stress of the valve, determination of the length of the leaflet at each point in Z according to a parabolic function not only minimises the formation of a belly in the leaflet, but also reduces the pressure gradient required to open the valve from a closed position.

The opening of a cardiac valve to as wide an orifice as possible under minimal pressure gradients is a key parameter in the design of synthetic heart valves.

The valve is produced such that in a cast position the leaflet is in neutral position, intermediate the

open and closed position in the absence of fluid pressure being applied to the leaflets. Production of the valve in the neutral position means that the leaflets are substantially free of bending stresses in this position.

The shape of the former on which the leaflet is formed is defined by either at least one wave or several waves which form a composite wave.

Regardless of the shape of the leaflet, the length of the leaflet is defined at each point in Z along the post of the scallop by a parabolic function as described above together with any correction factors.

The shape of the inner surface of the leaflets will substantially replicate the shape of the former. The shape of the outer surface of the leaflets will be similar to the shape of the inner surface, but variations will result e.g. from the properties of the polymer solution and techniques used to create the leaflet.

The leaflets of suitable length as defined by the parabolic function and any correction factors and of shape as defined by either a single or composite wave function are attached to a suitable frame. The construction of a suitable frame will be obvious to those skilled in the art. The frame can be made of a biocompatible polymer, metal or composite. The

frame can be coated with polyurethane to allow integration of the leaflets.

Further to describing a first leaflet using the above function, the remaining two leaflets of this three leaflet embodiment can be determined by rotating the geometry about the Z axis through 120° and then through 240°.

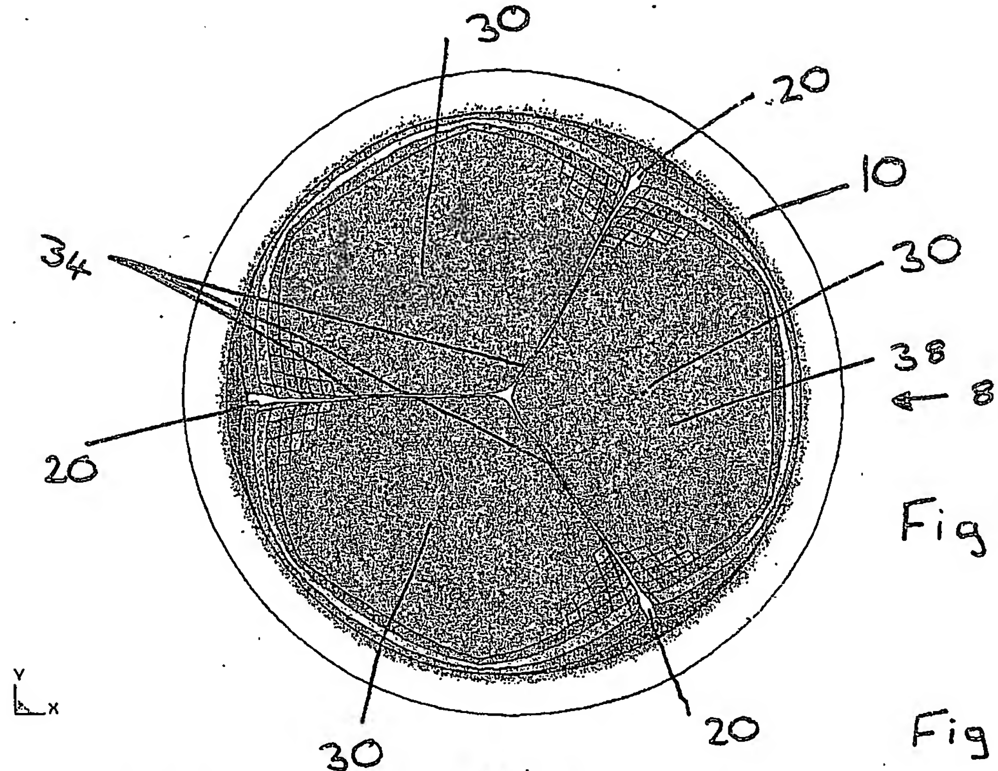
Having formed the leaflets of the valve as described above these can then be trimmed such that the edge of the leaflet not attached to the frame extends horizontally between two posts horizontally between a longitudinal length 0 to 1500μm beyond the tips of the posts of the frame. The edge of the leaflets which extends horizontally between the tips of the posts or between a longitudinal length 0 to 1500μm beyond the tip of the posts is deemed to be the notional free edge of the leaflets.

The notional free edge of the leaflet can be further trimmed in the longitudinal direction such that a parabolic curve is introduced, the maximum depth of the parabola being located between 50μm to 1000μm opposite the notional untrimmed free edge toward the portion of the leaflet which attaches the leaflet to the scallop portion of the frame.

A valve of the present invention may be used in any required position within the heart to control blood

flow in one direction, or to control flow within any type of cardiac assist device.

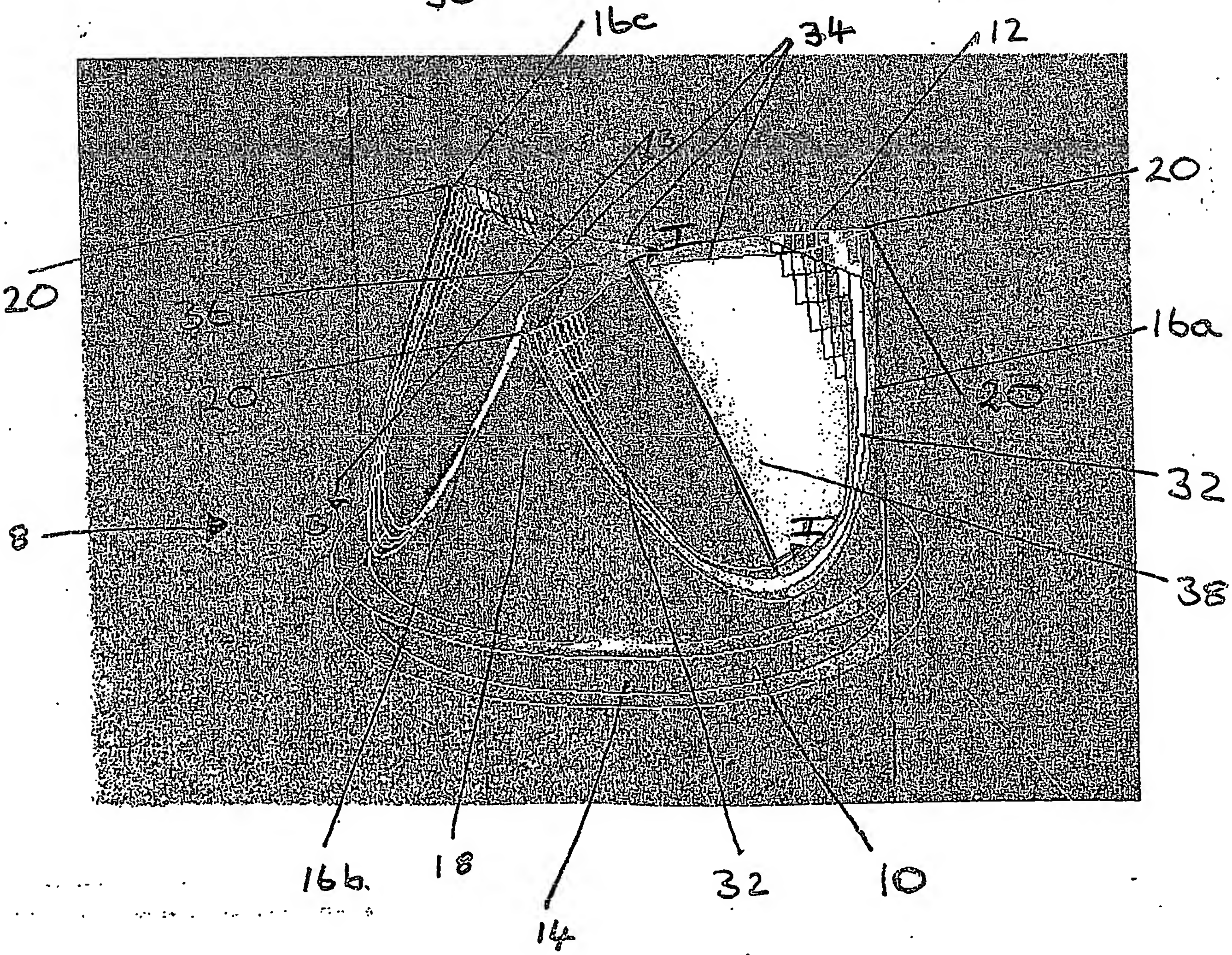
Modifications and improvements can be incorporated without departing from the scope of the invention.



30
20
10
34
30
38
8
20
30
20
Y
X

Fig 1

Fig.2a



16c
34
12
20
20
36
20
16a
20
32
8
38
16b.
18
32
10
14

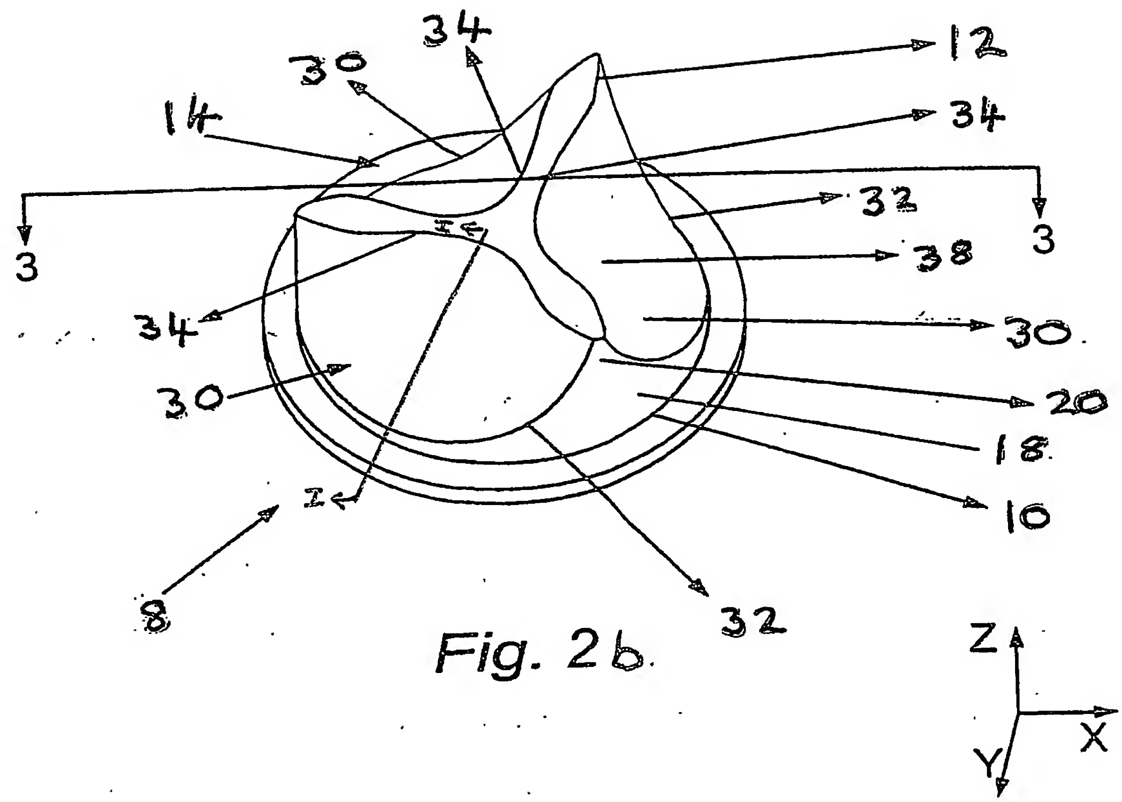


Fig. 2b

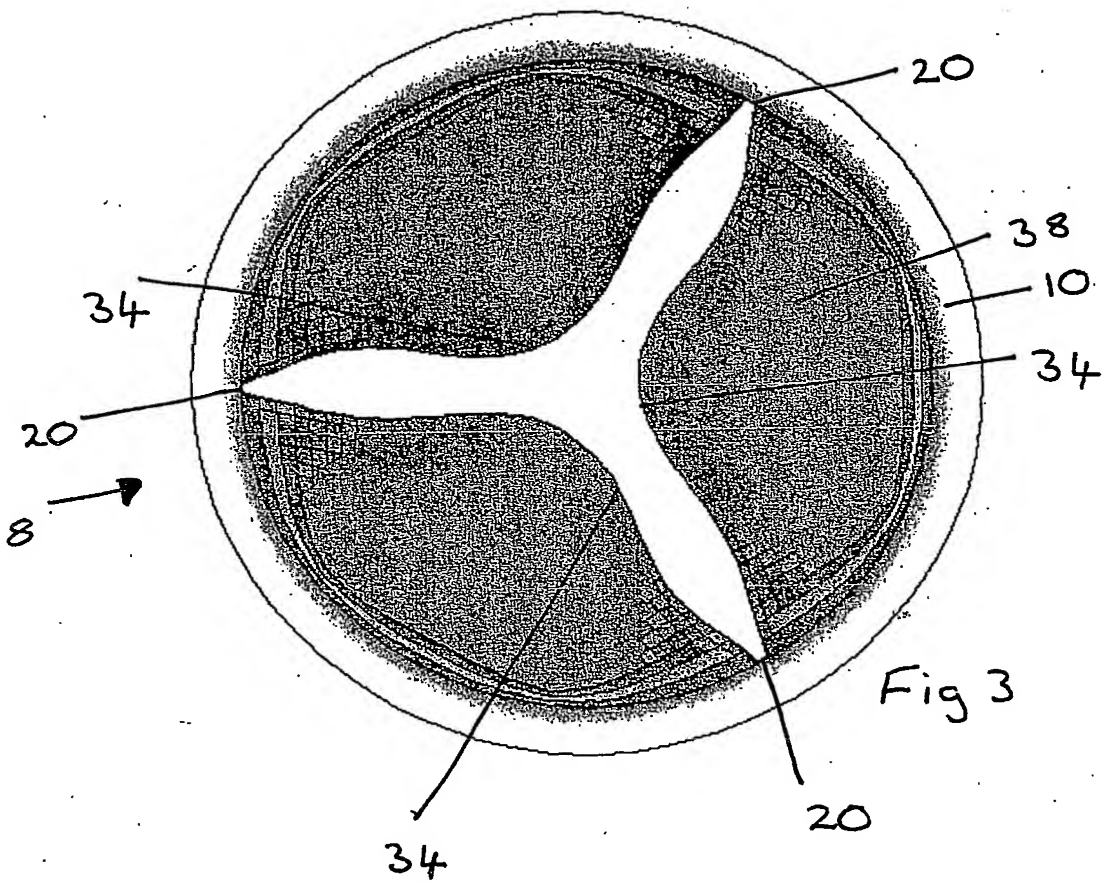


Fig 3

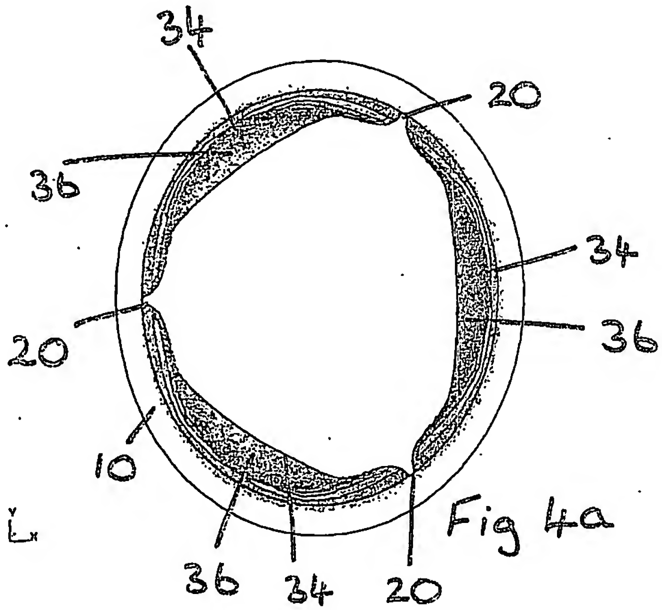


Fig 4a

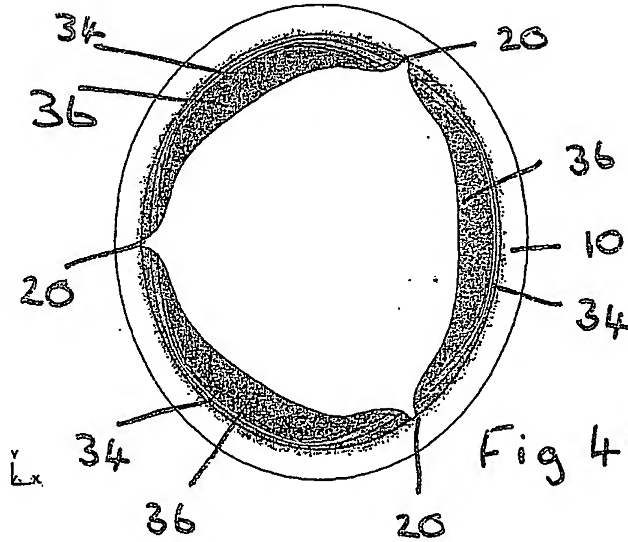


Fig 4c

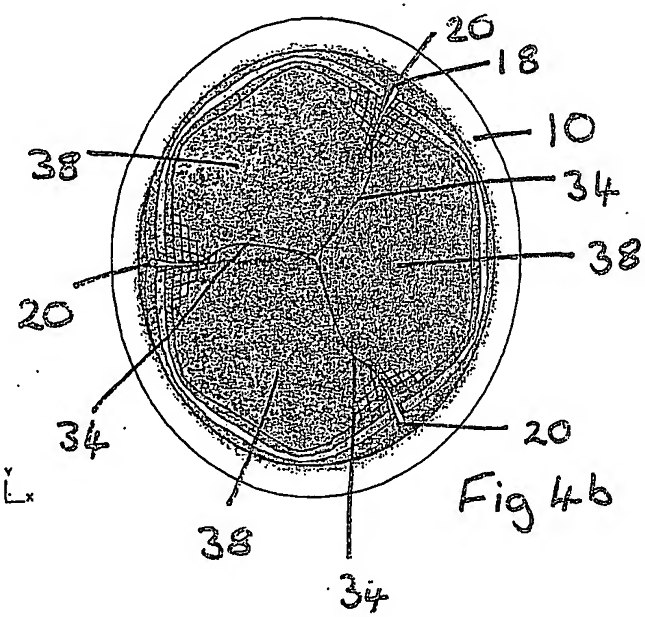


Fig 4b

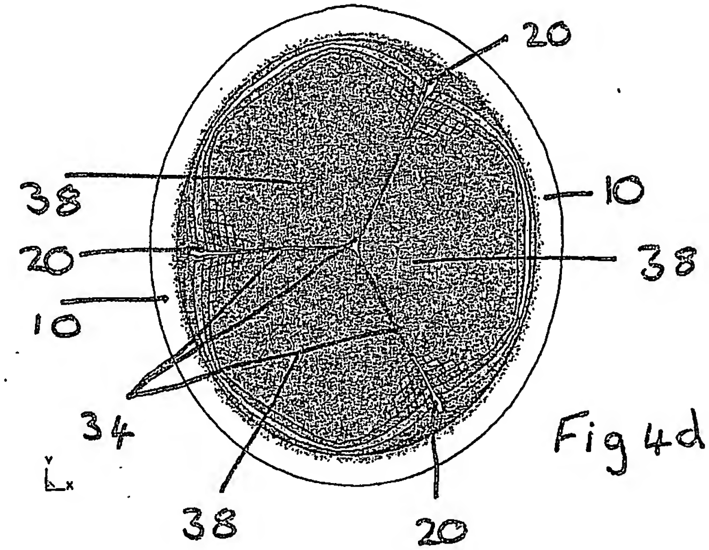


Fig 4d

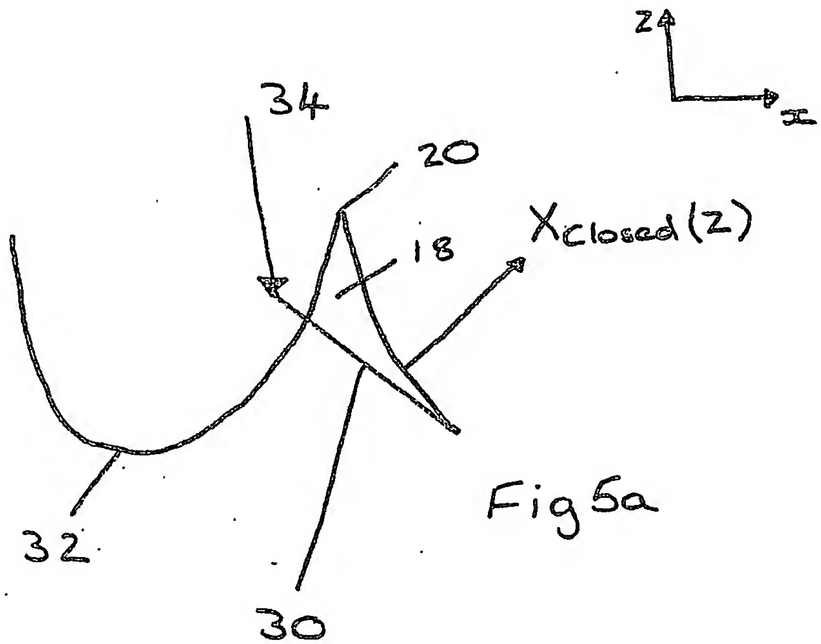


Fig 5a

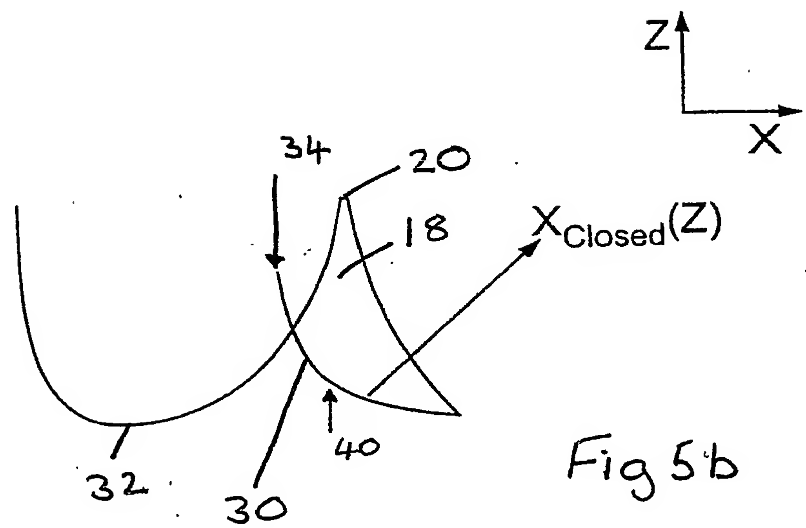


Fig 5b

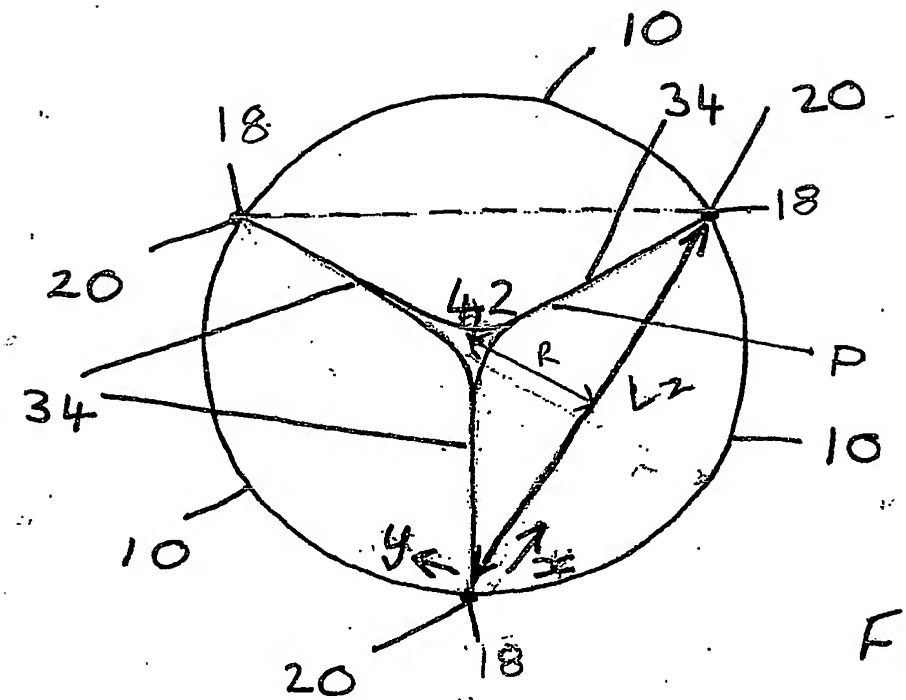


Fig 6

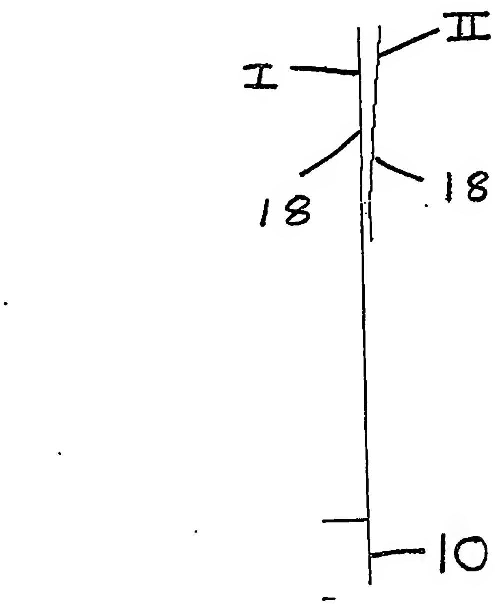


Fig 7a

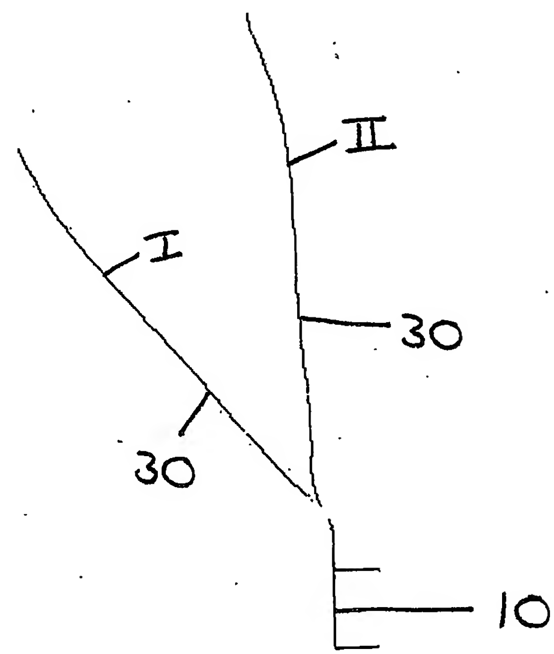


Fig 7b

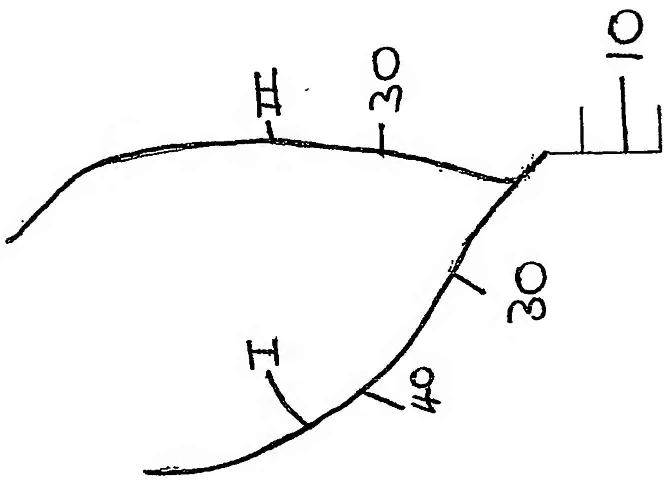


Fig 7d

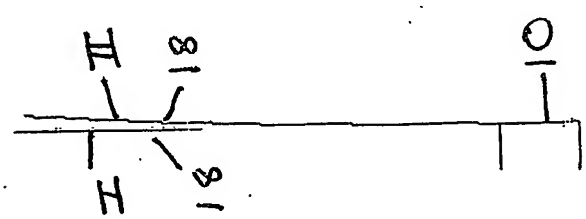


Fig 7c

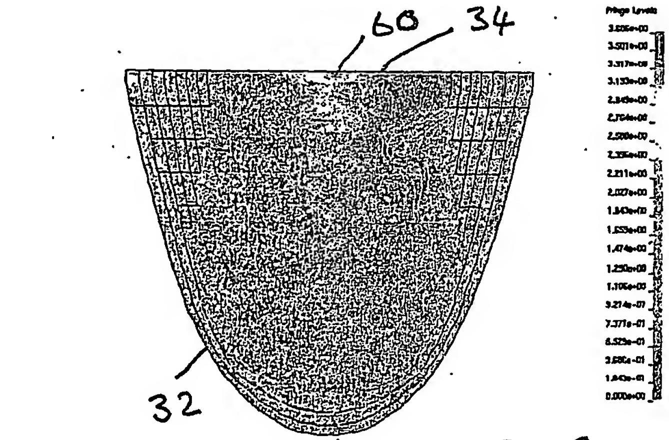


Fig 8a

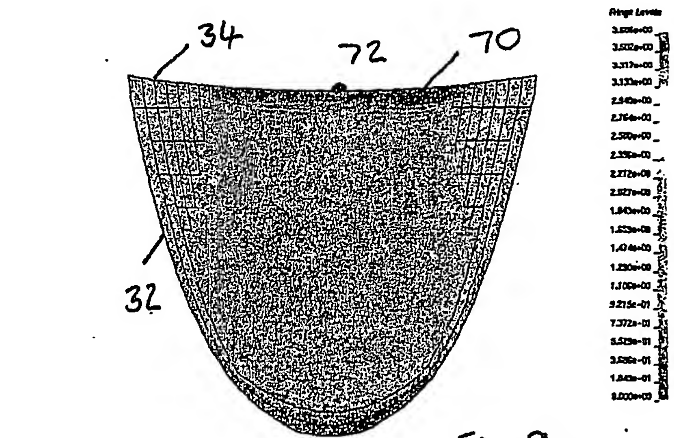


Fig 9a

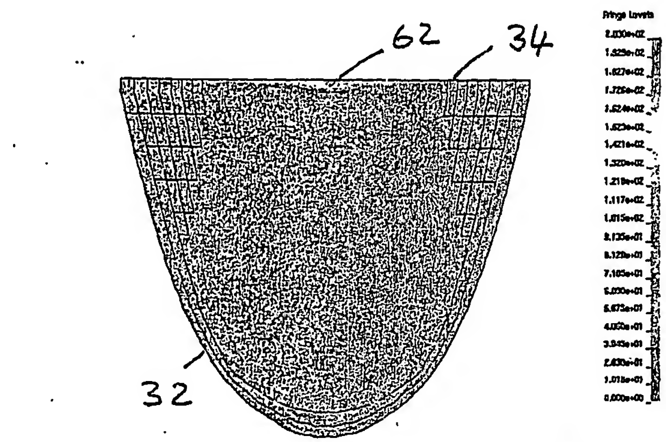


Fig 8b

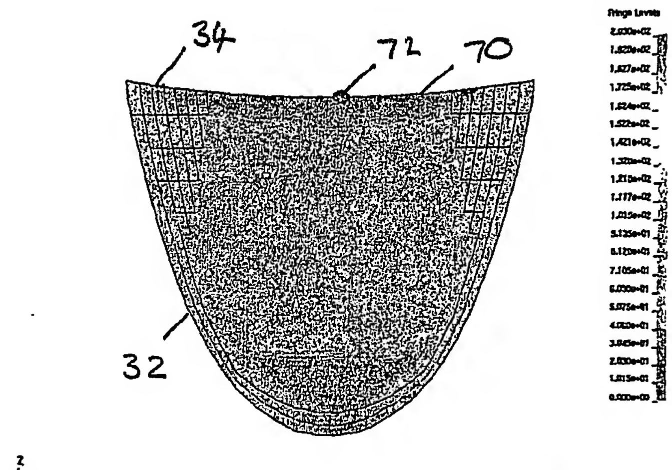


Fig 9b

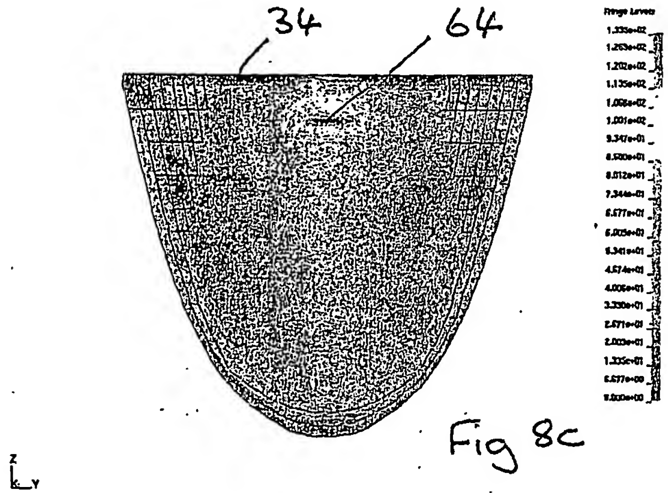


Fig 8c

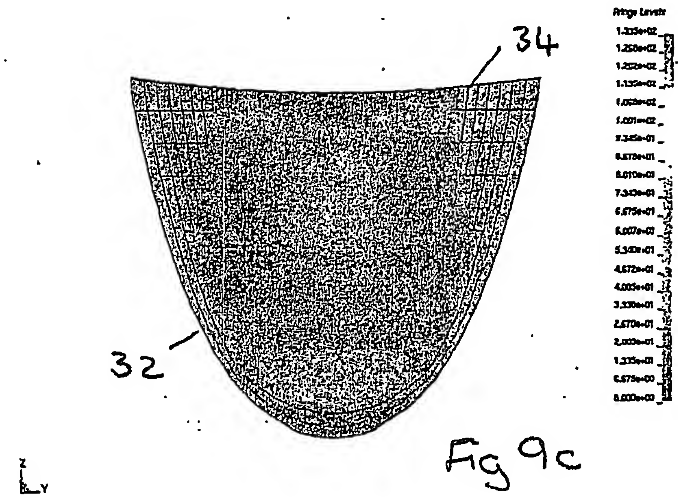


Fig 9c

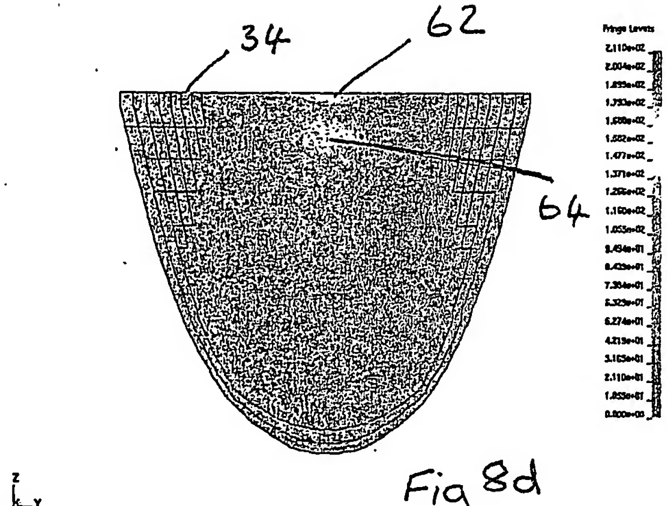


Fig 8d

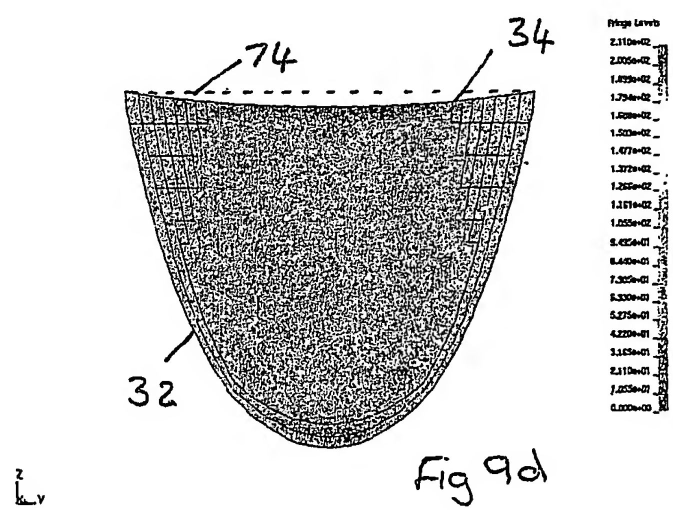


Fig 9d

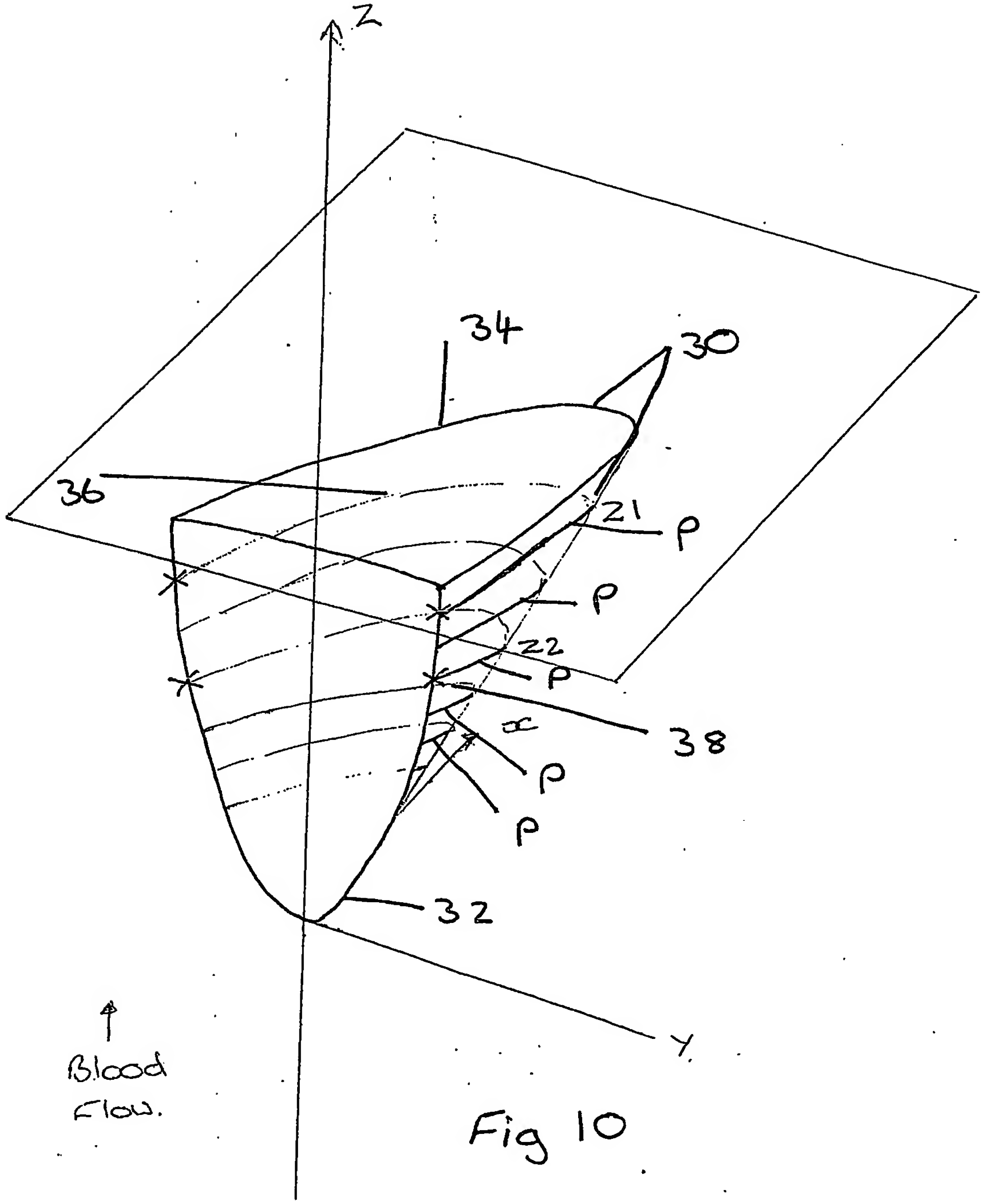
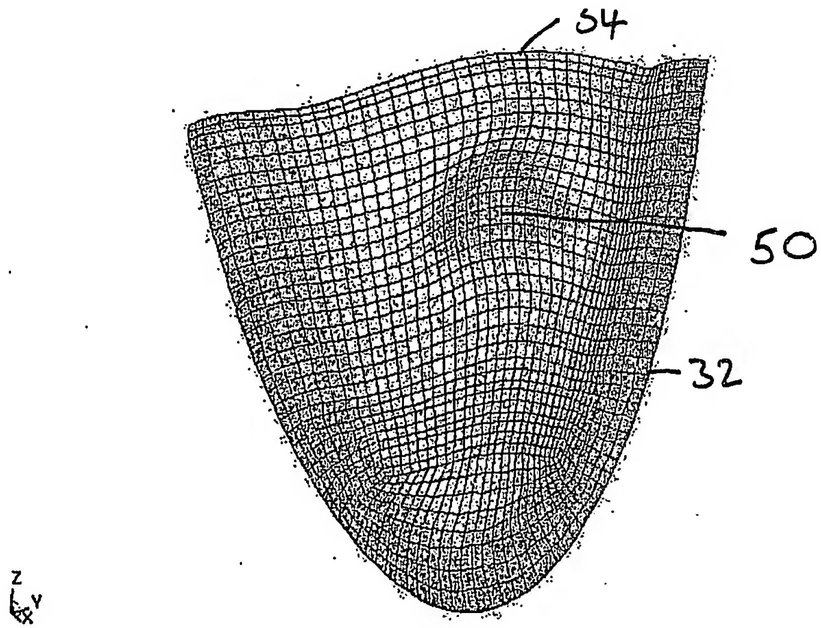
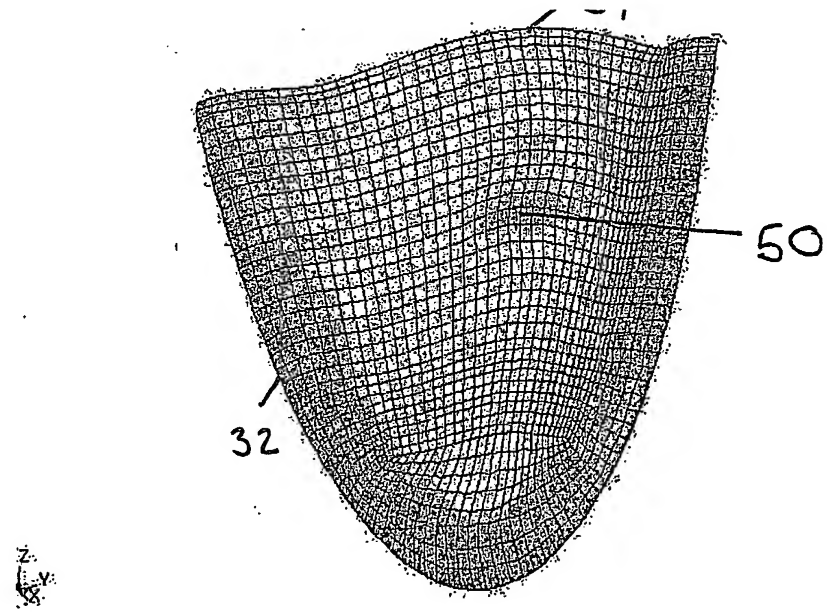


Fig 10



(a)



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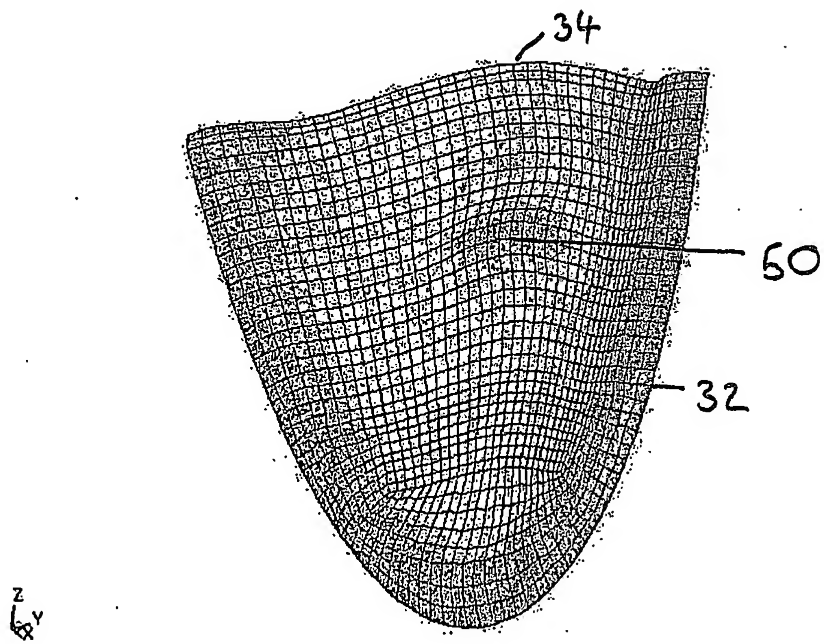

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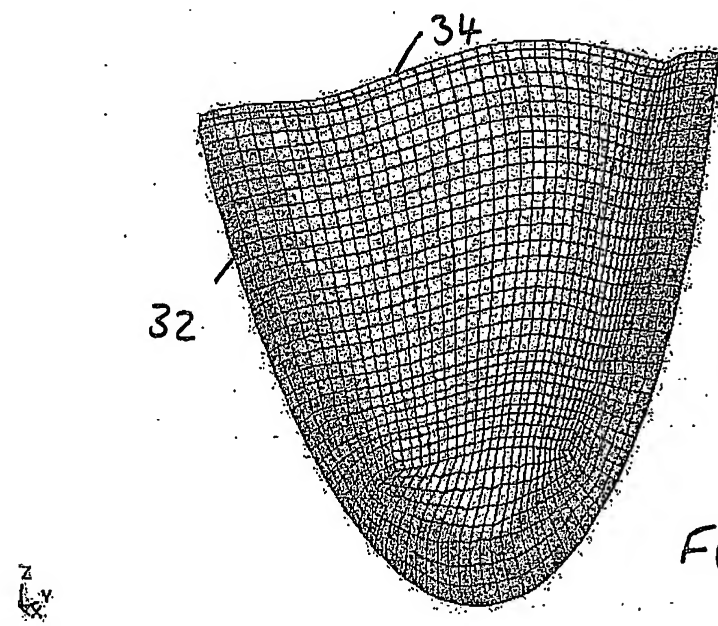

(d)

Fig 11

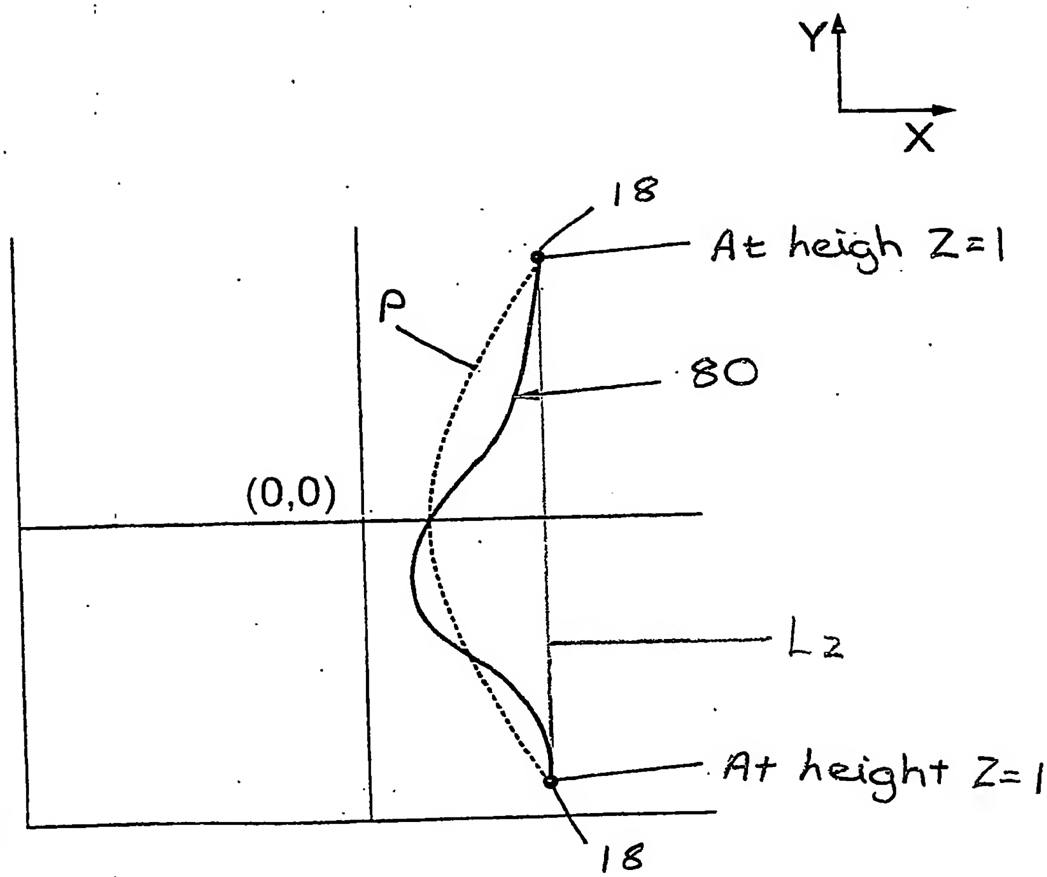

Fig. 12

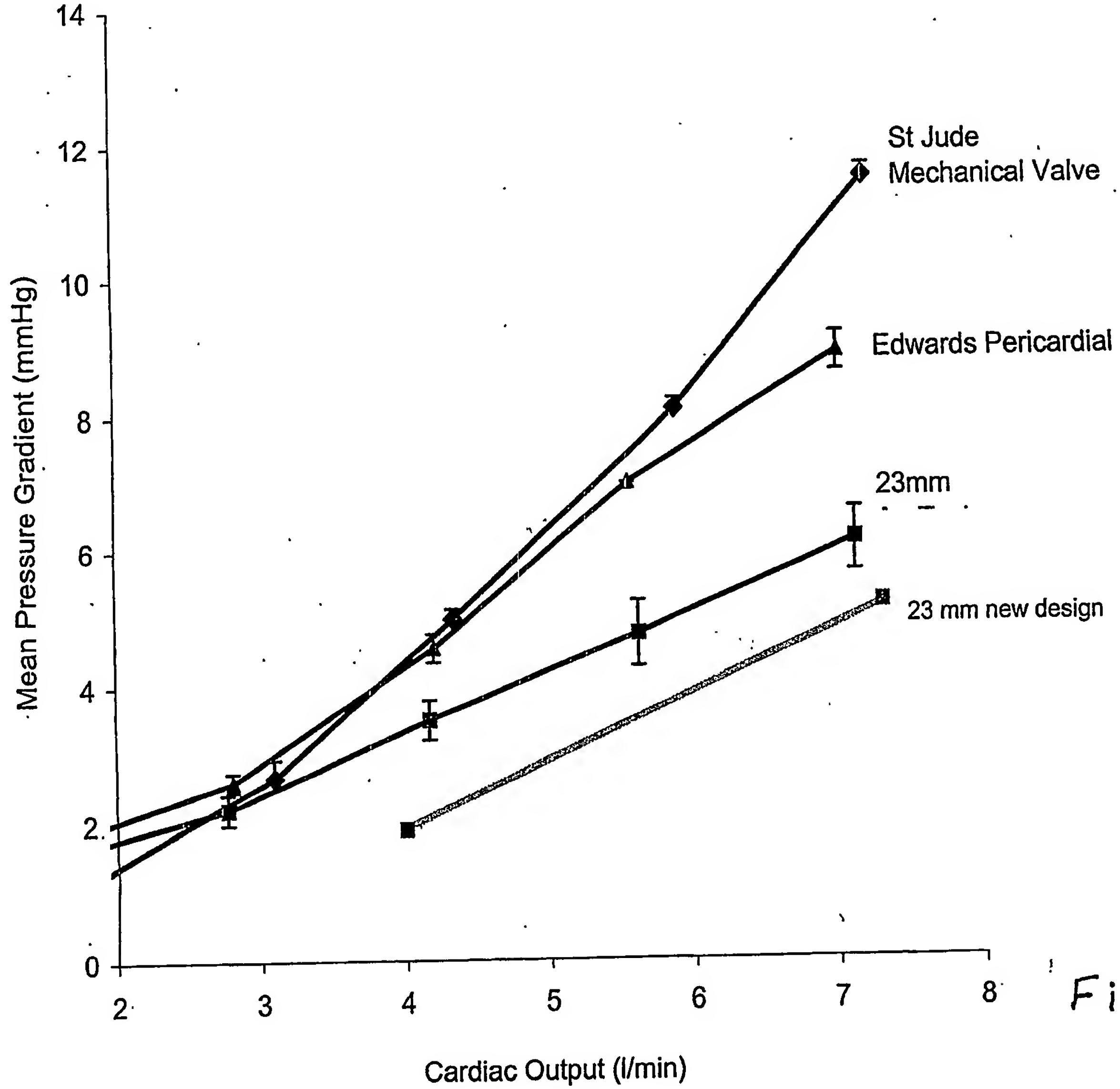
Mean Pressure Gradient (mmHg)
14
12
10
8
6
4
2
0
2
3
4
5
6
7
8
Cardiac Output (l/min)
St Jude
Mechanical Valve
Edwards Pericardial
23mm
23 mm new design

Fig 13